



TITLE:

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# **Suitability of the Montreal Cognitive Assessment versus the Mini-Mental State Examination in detecting vascular cognitive impairment**

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Short title: MoCA-J for vascular cognitive impairment

Author's contribution:

Masafumi Ihara; patient care, neuropsychological assessment, statistical analysis

Yoko Okamoto; neuropsychological assessment

Ryosuke Takahashi; study supervision

## Abstract

### Goal:

The Mini-Mental State Examination (MMSE) has been criticized as an insufficient screening test for patients with vascular cognitive impairment due to insensitivity to visuospatial and executive functional deficits. The Montreal Cognitive Assessment (MoCA) was designed to be more sensitive to such deficits and may therefore be a superior screening instrument for vascular cognitive impairment.

### Methods:

Twelve patients with extensive leukoariosis on magnetic resonance imaging ( $76.0 \pm 8.7$  yrs on average) underwent neurological and cognitive measures, including the Japanese version of MoCA (MoCA-J) and MMSE. Accepted cutoffs of MMSE  $<27$  and MoCA  $<26$  were taken to indicate cognitive impairment. Z scores were calculated to evaluate the discriminating ability of individual MMSE and MoCA-J subtest scores.

### Findings:

Although there was a strong correlation between the total MoCA-J and MMSE scores ( $r=0.90$ ,  $p<0.0001$ ), MMSE scores were skewed toward the higher scores (range 18-30, median 28), while MoCA-J scores

were normally distributed (range 9-28, median 21). Of the seven patients with unimpaired MMSE scores, six (86%) patients had an impaired MoCA-J score. Z scores were  $>5$  for four MMSE subtests (orientation, registration, naming, and language) but for only one MoCA-J subtest (naming).

#### Conclusions:

The MoCA-J better discriminated cognitive status between subjects with extensive leukoaraiosis.

MoCA-J is more sensitive than the MMSE in screening for cognitive impairment in patients with subcortical vascular cognitive impairment.

Keywords: leukoaraiosis, Montreal Cognitive Assessment, screening, stroke, vascular cognitive impairment

## 1. Introduction

Cognitive impairment resulting from cerebrovascular insufficiency has been termed vascular cognitive impairment (VCI).<sup>1</sup> VCI forms a spectrum that includes mild cognitive impairment of vascular etiology (vascular MCI), vascular dementia, mixed Alzheimer's disease with a vascular component.<sup>2, 3</sup> As vascular MCI patients with more severe impairment were found to be at higher risk of conversion to dementia, compared to patients with less severe or no cognitive impairment,<sup>4</sup> early detection of cognitive deficits may facilitate in preventing cognitive deterioration.

The widely used Mini-Mental State Examination (MMSE)<sup>5</sup> was found to be inaccurate in screening VCI as it was insensitive to MCI or complex cognitive deficits specifically.<sup>1, 6</sup> By comparison, the Montreal Cognitive Assessment (MoCA) has been designed to be sensitive to mild deficits<sup>7</sup> and has been evaluated in amnesic MCI<sup>7</sup> and Parkinson disease<sup>8</sup>. Importantly, MoCA is reported to detect more cognitive abnormalities after ischemic stroke or transient ischemic attack, compared to MMSE, particularly in relation to executive function, attention and delayed recall.<sup>9, 10</sup> In addition, the Hong Kong MoCA is reported to be useful for use in Chinese patients with leukoaraiosis;<sup>11</sup> however, direct comparison of MoCA with MMSE scores has not been performed in VCI.

Hence, the primary aim of the present study was to test the hypothesis that MoCA is more sensitive than MMSE in the detection of cognitive impairment in patients with ischemic leukoaraiosis, namely subcortical VCI, which incorporates two clinical entities ‘Binswanger’s disease’ and ‘the lacunar state’. The feasibility and the psychometric properties of MoCA (modified for Japanese population; MoCA-J) were compared with MMSE.

## 2. Methods

### Subjects

Twelve patients whose FLAIR- and T2-weighted MRI scans revealed confluent hyperintensities in the subcortical white matter (Schmidt scale score of 3)<sup>12</sup> and several punctate high-intensity areas in the basal ganglia were studied. The patients were enrolled because of the above neuroradiological abnormalities after visiting our Neurology Clinic from May 2008 to March 2011 with various neurologic signs and symptoms. Patients with mild to moderate leukoaraiosis (Schmidt scale score of 1 or 2) were not enrolled in this study to exclude the possibility of leukoaraiosis associated with neurodegenerative disorders, such as Alzheimer’s disease. Each subject was fully instructed on the experimental procedures and provided with written, informed consent, as approved by the Committee of Medical Ethics within our faculty. None

of the patients had apparent lesions in the cerebral cortex or hippocampus. MR angiography and duplex color-coded sonography did not reveal >50% stenosis in the major intracranial and extracranial vessels.

### Neuropsychological evaluation

All subjects underwent a general physical and neurologic examination and neuropsychological assessment, including the MoCA-J and MMSE. To avoid habituation and interference effects, MMSE was carried out at least one week after MoCA-J assessment. Two neurologists were involved in the neuropsychological assessment; if their assessments did not correlate, patients were reexamined by the team for a final verdict. A cutoff of  $\geq 27$  on MMSE score was chosen to indicate normal cognitive function<sup>13</sup> and the accepted cutoff of <26 on the MoCA-J was taken to indicate cognitive impairment.<sup>14</sup>

### The Z score analysis

For both the MMSE and MoCA-J subtests, the Z scores were calculated by dividing the mean subtest score by its standard deviation, where lower Z scores indicate greater discrimination between subjects.

### Statistical analysis

The statistical significance of intergroup differences was assessed with Fisher's exact test for categorical variables, and continuous variables of demographic data by the Mann-Whitney U test. Possible links

between the variables were observed using Pearson correlation analysis.

### 3. Results

#### Demographic data of the patients

Patient clinical features and demographics are summarized in the **Table 1**. All patients had at least 1 risk factor for ischemic cerebrovascular disease, including hypertension and diabetes mellitus. Eight of 12 patients (67%) showed gait disturbance, the most frequent neurological deficit. The mean modified Rankin Scale score was 1.4 (range, 1–2). Most of the patients showed lacunar infarctions or microbleeds in the basal ganglia or the thalamus as a manifestation of underlying small vessel pathology. Their clinical histories and radiological features excluded possibility of co-existing single-strategic infarct dementia.

#### Relationship between MoCA-J and MMSE scores

There was a significant relationship between the MoCA-J and MMSE scores ( $r=0.90$ ,  $p<0.0001$ ). MMSE scores were skewed toward the higher scores (range 18–30, median 28) while MoCA-J scores were normally distributed (range 9–28, median 21) (Figure 1). Of the 11 patients with impaired MoCA-J scores, only five (45%) patients had an impaired MMSE score, while all 11 patients with impaired MMSE scores



had an impaired MoCA-J score. Of the seven patients with unimpaired MMSE scores, six (86%) had an impaired MoCA-J score.

#### Z score analysis

Individual subtests of the MMSE and MoCA-J, together with the results, are described in **Table 2** and **Table 3**, respectively. Z scores were  $>5$  for four MMSE subtests (orientation, registration, naming, and language) but only for one MoCA-J subtest (naming).

#### Clinical utility of the MoCA-J

The MoCA-J was accomplished by all the Japanese elderly subjects with VCI enrolled in this study. The average administration time was 12 minutes.

#### Correlation analysis between the MoCA-J score and the MRI-based cerebrovascular lesions

The MoCA-J score was significantly correlated with the number of lacunar infarctions ( $r=-0.67$ ,  $p=0.03$ ) but not with the number of microbleeds in the basal ganglia or the thalamus ( $r=-0.39$ ,  $p=0.28$ ).

#### 4. Discussion

The main finding of this study is that MoCA-J is more sensitive than the MMSE in detecting subcortical VCI. Eleven of the 12 patients with either impaired MoCA-J or MMSE scores could only be detected by impaired MoCA-J scores, while none of the patients presented with only impaired MMSE scores. In addition, the Z score analysis suggested that the MoCA-J better discriminated cognitive status between subjects. Therefore, MoCA-J could be a useful instrument to detect VCI at an earlier stage in patients with extensive leukoaraiosis. The significant correlation of the MoCA-J score with the number of lacunar infarctions further suggests the clinical relevance of this screening test in the detection of VCI characterized by small vessel pathology. It took only 12 minutes to administer the MoCA-J even in subcortical VCI patients.

The poorer performance of the MMSE in detecting subcortical VCI may be due to several factors. The MMSE is less sensitive in detecting impairment in visuospatial or executive function, characteristic features that are preferentially impaired in VCI.<sup>2, 15</sup> In light of such restrictions of MMSE, the trail-making test or digit symbol test has been recommended to supplement the MMSE to improve its sensitivity in the cognitive assessment of subjects with leukoaraiosis.<sup>16</sup> Furthermore, visuo-executive dysfunction has been found to predict poor survival after stroke;<sup>17</sup> therefore, early detection of VCI with MoCA is ideal for earlier initiation of intervention and improved outcome. Vascular risk factors should be adequately controlled to achieve a reduction in the risk of dementia.<sup>18</sup>

The MoCA-J demonstrated deficits in other cognitive domains, such as recall and language. As the specific assessment criteria to test recall and language are less complicated in MMSE than in MoCA-J, the ceiling effect may prevent MMSE from detecting intersubject differences in cognitive impairment. In support of this, the Z scores for recall and language in MoCA-J were lower than those in MMSE, indicating higher discriminating power of MoCA-J in assessment of cognitive impairment.

Recently, vascular risk factors have been reported to promote conversion from MCI to Alzheimer's disease.<sup>19</sup> Moreover, in patients who have clinically diagnosed Alzheimer's disease, treatment of vascular risk factors is associated with a slower decline in MMSE score.<sup>20</sup> A recent animal study has suggested that the effect of Alzheimer's neurodegeneration and VCI are not only additive but also synergistic in worsening cognitive impairment.<sup>21</sup> Therefore, the early diagnosis of amnesic MCI with MoCA<sup>7, 14</sup> may also benefit patients by the introduction of optimal control of any vascular risk factors, which may prevent conversion of MCI to dementia.

The main limitation is a small number of patients enrolled in this study as only those with most severe white matter changes were eligible for this study to minimize heterogeneity of VCI and to exclude those with white matter changes secondary to neurodegenerative changes to the utmost extent.<sup>22</sup> This

preliminary study should therefore be viewed as hypothesis generating and should be followed by larger studies to confirm the results. Nevertheless, our study provided a direct comparison of MMSE and MoCA-J, which showed an appreciably greater suitability of the MoCA-J against the MMSE in the detection of VCI.

In conclusion, the MoCA-J is a promising tool for the screening for cognitive impairment in VCI patients with leukoariosis as it may detect complex cognitive impairments, such as in executive function and visual perception, at earlier stages of VCI.

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**Table 1. Patient clinical features and demographics**

Variable	
Mean age (range), y	76±8.7 (55–84)
Gender	M, 7; F, 5
Modified Rankin Scale, mean score (range)	1.4±0.5 (1–2)
Gait disturbance, No. (%)	8 (67)
Dysarthria, No. (%)	4 (33)
Urinary incontinence, No. (%)	3 (25)
Hypertension, No. (%)	7 (58)
Diabetes mellitus, No. (%)	3 (25)
Cigarette smoking, No. (%)	3 (25)
Sleep apnea, No. (%)	2 (17)
Previous CVD, No. (%)	6 (50)
Use of antithrombotics, No. (%)	8 (67)
Use of statins, No. (%)	6 (50)
LDL Cholesterol, mg/dL	115±44
Triglyceride, mg/dL	112±45



Hematocrit, %	39.6±3.9
Fibrinogen, mg/dL	286±53
No. of MBs in the BG/thalamus	1.5±2.0
No. of lacunas in the BG/thalamus	2.9±2.8

BG, basal ganglia; CVD, cerebrovascular disease; MBs, microbleeds

**Table 2. Mean of MoCA-J subtest scores with different cognitive screening test results**

MOCA-J	Visuo- executive/5	Naming/3	Attention/6	Language/3	Abstraction/2	Recall/5	Orientation/6
Pt 1	1	2	4	1	1	0	5
Pt 2	1	3	3	0	0	0	2
Pt 3	3	3	6	1	2	3	6
Pt 4	2	3	3	1	2	0	4
Pt 5	3	2	6	2	1	4	5
Pt 6	4	3	5	2	2	3	6
Pt 7	3	3	6	1	1	2	6
Pt 8	4	3	5	1	1	0	6
Pt 9	2	3	6	2	2	0	6
Pt 10	5	3	6	2	2	4	6
Pt 11	3	3	5	1	0	0	5
Pt 12	2	3	6	2	2	0	4
Average	2.8	2.8	5.1	1.3	1.3	1.3	5.1
SD	1.2	0.4	1.2	0.7	0.8	1.7	1.2
Z score	2.3	7.3	4.4	2.0	1.7	0.8	4.1

MoCA-J domain subtest maximum score/details: visuo-executive/5 – trail B test, cube copy, clock

drawing; attention/6 – digit span, vigilance (tapping at the Hiragana ‘a’ in a list of Hiragana characters),

serials 7 s; recall/5 – recall a list of 5 words; orientation/6 – date, month, year, day, place, city;

abstraction/2 – similarities between two items; language/3 – sentence repetition, verbal fluency; naming/3

– confrontation naming (lion, rhino, camel).

**Table 3. Mean of MMSE subtest scores with different cognitive screening test results**

MMSE	Orientation/10	Registration/3	Attention/ Calculation/5	Recall/3	Naming/2	Language/6	Drawing/1
Pt 1	9	3	4	2	2	3	0
Pt 2	5	2	4	0	1	5	1
Pt 3	10	3	5	3	2	6	1
Pt 4	10	3	1	0	2	5	1
Pt 5	10	3	4	2	2	5	1
Pt 6	10	3	5	2	2	6	1
Pt 7	10	3	5	3	2	6	1
Pt 8	10	3	4	0	2	6	1
Pt 9	10	3	4	3	2	6	1
Pt 10	10	3	5	3	2	6	1
Pt 11	10	3	1	0	2	6	1
Pt 12	9	3	5	3	2	6	1
Average	9.4	2.9	3.9	1.8	1.9	5.5	0.9
SD	1.4	0.3	1.4	1.4	0.3	0.9	0.3
Z score	6.5	10.1	2.7	1.3	6.6	6.1	3.2

MMSE domain subtest maximum score / details: attention/calculation/5 – serial 7 s; recall/3 – recall a list of 3 words; orientation/10 – orientation to place and time; naming/2 – confrontation naming (pen, watch); language/6 – sentence repetition, comprehension, reading, writing; registration/3 – repeat 3 words; praxis/1 – copy intersecting pentagons.

### Figure legends

Figure 1. Distribution of MoCA-J and MMSE scores of the patients with extensive leukoaraiosis. Cutoffs of MMSE <27 and MoCA-J <26 were taken to indicate cognitive impairment (dotted line).